

REMARKS

Upon entering the above amendments to the claims, claims 1-4, 10-12, 18-44 and 46-48 will be pending in this application and are presented for examination. Claims 1-4 and 10-12 have been withdrawn from consideration by the Examiner. Claims 18-47 stand rejected. Claim 45 is now canceled by Applicants without forfeiting any right to pursue canceled subject matter in a subsequent divisional or continuation application. Claims 18 and 23-24 have been amended. New claim 48 has been added.

Reconsideration of the application is respectfully requested in view of the above amendments to the claims and the following remarks. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

Amendments to claims 18 and 23-24 are meant to correct minor typographical errors only.

Re-presented claim 48 incorporates the subject matter of canceled claim 45 as well as the subject matter of compound claim 1.

Applicants believe no new matter is present in this or any other portion of the present amendment.

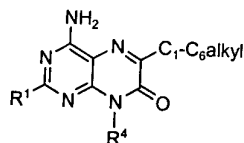
I. Objection to Claim 45

The Examiner has objected to claim 45 as depending from non-elected claim 1. Applicants note that claim 45 has been canceled, and has been re-presented in independent format as claim 48. Re-presented claim 48 incorporates the subject matter of both canceled claim 45 and withdrawn claim 1. As such, Applicants respectfully submit that the objection has been rendered moot.

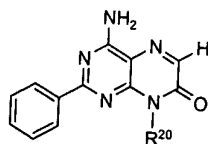
II. Claims of the Instant Application are Novel in view of WO 98/26093

The Examiner has rejected claims 18-47 of the present application under 35 U.S.C. § 102(a) in view of Hawkins *et al.* (WO 98/26093, the '093 publication). In response, Applicants respectfully traverse the rejection.

The '093 publication discloses Formulas (IX) and (X), wherein one of R¹ and R³ of the present application is phenyl when R⁴ (R²⁰ in the '093 publication) is ribose or deoxyribose:



Instant application



(IX)



(X)

Applicants note for the Examiner's convenience, that the pteridine nucleotides of the instant application have *only* an alkyl group at the 6 position (R³) of the pteridine ring. In sharp contrast to the instant application, the pteridine nucleotides of the '093 publication have either a *phenyl* or a *hydrogen* at the 6 position of the pteridine ring. Applicants respectfully submit that an alkyl group is not equivalent to a hydrogen or a phenyl ring, and thus, the claims of the instant application are *not* anticipated by the '093 publication.

Furthermore, the pteridine nucleotides of the instant application *must* be attached to an adenosine moiety through the phosphates at one of R⁶ and R⁷. In contrast, the '093 publication recites simply a phosphate for these positions without any disclosure as to what the phosphates are attached to. As the Examiner is aware, MPEP § 2131 recites:

To anticipate a claim, the reference must teach every element of the claim

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

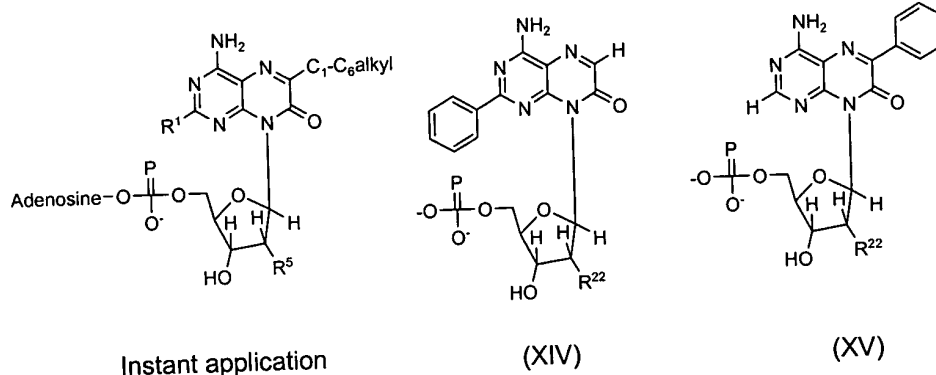
As such, Applicants respectfully submit that the '093 publication does *not* teach all the elements of the claims of the instant application. Accordingly, Applicants respectfully request that the rejection be withdrawn.

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III. Claims of the Instant Application are Novel in view of WO 95/31469

The Examiner has rejected claims 18-27 and 46-47 of the instant application under 35 U.S.C. § 102(b) as allegedly being anticipated by Hawkins *et al.* (WO 95/31469). The Examiner alleges that "[t]he reference discloses pteridine nucleotides (pages 3-4, 23-30) which are viewed to be identical to the instant invention." In response, Applicants respectfully traverse the rejection.

Hawkins *et al.* disclose Formulas (XIV) and (XV) wherein one of R¹ and R³ of the present application is phenyl when R⁴ is ribose (R⁵ is OH, R²² of Hawkins *et al.* is OH) or deoxyribose (R⁵ is H, R²² of Hawkins *et al.* is H):



As discussed above, the pteridine nucleotides of the instant application have *only* an alkyl group at the 6 position (R³) of the pteridine ring. In sharp contrast to the instant application, the pteridine nucleotides of Hawkins *et al.* have either a *phenyl* or a *hydrogen* at the 6 position of the pteridine ring. Applicants respectfully submit that an alkyl group is not equivalent to a hydrogen or a phenyl ring, and thus, the claims of the instant application are *not* anticipated by Hawkins *et al.*

Furthermore, the pteridine nucleotides of the instant application *must* be attached to an adenosine moiety through the phosphates at one of R⁶ and R⁷. In contrast, Hawkins *et al.* recites simply a phosphate for these positions. As the Examiner is aware, the cited reference must teach each and every element of the claim, MPEP § 2131. Applicants respectfully submit that Hawkins *et al.* does *not* teach all the elements of the claims of the instant application. Accordingly, Applicants respectfully request that the rejection be withdrawn.

IV. Claims of the Instant Application are Novel in view of Jungmann *et al.*

The Examiner has rejected claims 18 and 20 of the instant application under 35 U.S.C. § 102(b) as allegedly being anticipated by Jungmann *et al.*, *Nucleosides & Nucleotides* 1997, 16(5&6), 863. The Examiner alleges that "[t]he reference discloses pteridine nucleosides [*sic*] analogs as building blocks for oligonucleotides [*sic*] synthesis." Applicants respectfully traverse the rejection.

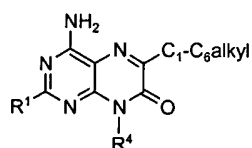
Applicants respectfully submit that Jungmann *et al.* teach *only* compounds to be used in preparing oligonucleotides, *not* the actual oligonucleotides themselves. Applicants respectfully submit that the Examiner is reading into the reference subject matter that is not contained therein, taking the objectives and intent of the instant application and improperly applying them to Jungmann *et al.* In so doing, the Examiner is using impermissible hindsight reconstruction. There is no disclosure or teaching in Jungmann *et al.* about how to prepare an oligonucleotide incorporating the compounds therein, nor is there any disclosure of preferred oligonucleotide sequences. In addition, Jungmann *et al.* does not disclose that when incorporated in an oligonucleotide, the pteridine nucleoside is attached to at least one adenosine, as is presently claimed. As the Examiner is aware, the cited reference must teach each and every element of the claim, MPEP § 2131. Accordingly, Applicants submit that the claims of the instant application are not anticipated by Jungmann *et al.*, and respectfully request that the rejection be withdrawn.

V. Small Perturbations have Surprising Results

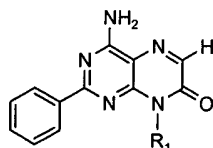
Applicants submit for the foregoing reasons that the pteridine rings of the instant invention are novel in view of the '093 publication, Hawkins *et al.* and Jungmann *et al.*

Moreover, the instant invention is unobvious. For example, the Examiner's attention is respectfully directed to probes 1 and 2 in reference AE, Hawkins *et al.* *Analytical Biochemistry* 1996, 244, 86. Probe 2, wherein R¹ is hydrogen, R³ is phenyl, and R⁴ is ribose, has a quantum yield of 0.16.

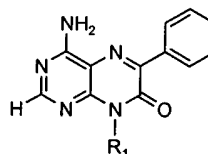
In contrast, the modifications to the pteridine rings claimed herein have surprising and advantageous effects. The instant application discloses that the pteridine rings of the present invention "are highly fluorescent, stable and easy to use." (Page 43, line 3.) The phenyl groups at positions 2 and 6 of the pteridine ring of probes 1 and 2 of Hawkins *et al.* are bulky, and likely to cause severe steric perturbations when incorporated into a strand of DNA. However, replacing the phenyl groups with simple hydrogen groups at positions 2 and 6 of the pteridine ring resulted in a structure with severe instability.



Instant application



Probe 1



Probe 2

In contrast to the unstable probes 1 and 2, the pteridine rings of the present invention are substituted with methyl groups where the 2 or 6 position of the pteridine ring is substituted with a phenyl. These molecules are as stable as probes 1 and 2 and display the surprising benefit of increased fluorescence intensity. In the case of probe 2 and 6MAP (R^1 of the instant invention is H, and R^3 is methyl), there is a 2.4 fold increase in quantum yield. In view of such an increase in quantum yield, the compounds of the instant invention have surprising and advantageous properties over the compounds of the cited references. As such, Applicants respectfully submit that the instant invention is unobvious in view of the '093 publication, Hawkins *et al.* and Jungmann *et al.* and that the rejection is moot.

VI. Obviousness-Type Double Patenting Rejection

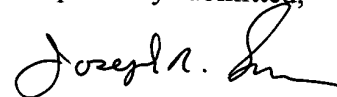
Upon notification of allowable subject matter in the instant application, Applicants will file a terminal disclaimer under 37 CFR § 1.321(c) to overcome the obviousness-type double patenting rejection in view of claims 16-17 of U.S. Patent No. 6,451,530.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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